

Applicants: Ira Tabas et al.
Serial No.: 10/646,412
Filed : August 22, 2003
Page 2

In the claims:

Please replace the pending claims with the listing of claims set forth below:

1. (original) A method for treating a subject suffering from a condition associated with an extracellular zinc sphingomyelinase activity which comprises administering to the subject an amount of a zinc sphingomyelinase inhibitor effective to decrease extracellular zinc sphingomyelinase activity in the subject and thereby treat the subject.
2. - 16. (cancelled)
17. (original) A method for determining whether a compound inhibits an activity of an extracellular zinc sphingomyelinase involving ceramide formation which comprises:
 - (a) contacting a sample containing the zinc sphingomyelinase under acidic pH conditions known to be associated with the activity of such zinc sphingomyelinase, with:
 - (i) a substrate of the zinc sphingomyelinase, and
 - (ii) the compound being evaluated;
 - (b) measuring the concentration of ceramide in the sample from (a);

Applicants: Ira Tabas et al.
Serial No.: 10/646,412
Filed : August 22, 2003
Page 3

(c) determining the amount of zinc sphingomyelinase activity in the sample based upon the concentration of ceramide measured in step (b); and

(d) comparing the amount of sphingomyelinase activity determined in step (c) with the amount of sphingomyelinase activity determined in the absence of the compound, so as to determine whether the compound inhibits the activity of zinc sphingomyelinase.

18. - 22. (cancelled)

23. (original) A method for determining whether a compound inhibits an activity of an extracellular zinc sphingomyelinase involving ceramide formation which comprises:

(a) contacting a sample containing the zinc sphingomyelinase under neutral pH conditions known to be associated with the activity of such zinc sphingomyelinase, with:

(i) a substrate of the zinc sphingomyelinase, and

(ii) the compound being evaluated;

(b) measuring the concentration of ceramide in the sample from (a);

Applicants: Ira Tabas et al.
Serial No.: 10/646,412
Filed : August 22, 2003
Page 4

- (c) determining the amount of zinc sphingomyelinase activity in the sample based upon the concentration of ceramide measured in step (b); and
 - (d) comparing the amount of sphingomyelinase activity determined in step (c) with the amount of sphingomyelinase activity determined in the absence of the compound, so as to determine whether the compound inhibits the activity of zinc sphingomyelinase.
24. (original) A method for screening a library of compounds to identify a compound capable of inhibiting an activity of zinc sphingomyelinase involving ceramide formation which comprises:
- (a) contacting a zinc sphingomyelinase under acidic pH conditions known to be associated with the activity of such zinc sphingomyelinase, with:
 - (i) a substrate of sphingomyelinase, and
 - (ii) a sample from a library of compounds being evaluated;
 - (b) measuring the concentration of ceramide in the sample from (a); and
 - (c) determining the amount of zinc sphingomyelinase

Applicants: Ira Tabas et al.
Serial No.: 10/646,412
Filed : August 22, 2003
Page 5

activity in the sample based upon the concentration of ceramide measured in step (b); and

(d) comparing the amount of sphingomyelinase activity determined in step (c) with the amount of sphingomyelinase activity determined in the absence of the sample, so as to determine whether the sample inhibits the activity of zinc sphingomyelinase, and

(d) repeating steps (a) through (d) with limiting dilutions of the sample so as to identify the compound in the sample capable of inhibiting zinc sphingomyelinase.

25. (original) A method for determining whether a subject is at increased risk for becoming afflicted with an increase in the concentration of extracellular zinc sphingomyelinase activity in the subject which comprises:

(a) obtaining a sample of a body fluid from the subject;

(b) determining the amount of extracellular zinc sphingomyelinase activity in the body fluid sample, and

(c) comparing the amount of extracellular zinc sphingomyelinase activity determined in step (a) with the amounts of extracellular zinc sphingomyelinase activity determined for the subject at earlier points

Applicants: Ira Tabas et al.
Serial No.: 10/646,412
Filed : August 22, 2003
Page 6

in time, an increase in the amount of such activity indicating that the subject is at increased risk for such condition.

26. - 29. (cancelled)

30. (original) A method for determining whether a subject has lipoproteins susceptible to extracellular zinc sphingomyelinase activity and thus is at increased risk for becoming afflicted with a condition associated with extracellular zinc sphingomyelinase activity which comprises:

- (a) obtaining a sample of a body fluid from the subject;
- (b) isolating the lipoproteins present in the sample;
- (c) contacting the isolated lipoproteins with zinc sphingomyelinase enzyme under acidic pH conditions known to be associated with the activity of such zinc sphingomyelinase;
- (d) measuring the concentration of ceramide in step (c), thereby determining whether the subject has lipoproteins susceptible to extracellular zinc sphingomyelinase so as to determine whether the subject is at increased risk for becoming afflicted with a condition associated with extracellular zinc sphingomyelinase activity.

Applicants: Ira Tabas et al.
Serial No.: 10/646,412
Filed : August 22, 2003
Page 7

31. - 34. (cancelled)

35. (original) A pharmaceutical composition comprising an amount of an inhibitor of an extracellular zinc sphingomyelinase effective to inhibit the activity of such zinc sphingomyelinase in a subject and a pharmaceutically acceptable carrier.

36. - 38. (cancelled)